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09/430,590	10/29/1999	RUSSELL TONY MASELL POULTER	674521-2001.	7513

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/430,590	POULTER ET AL.	
	Examiner	Art Unit	
	Gerald G Leff rs Jr., PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 35-50* is/are pending in the application.

4a) Of the above claim(s) *7,8,15,16 and 22-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-14,17,18 and 35-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 9/17/03, in which several claims were amended (claims 1-6, 10-12, 17-18, 20-21, 35), claims were cancelled (claims 33-34) and new claims were added (claims 37-50). Claims 1-32, 35-50 are pending, with claims 7-8, 15-16, 22-32 withdrawn from consideration as being directed to nonelected inventions.

Any rejection of record in the previous office action not addressed herein is withdrawn. This action is not final due to new grounds of rejection made herein that were not necessitated by applicants' amendment of the claims in the response filed 9/17/03.

Drawings

Applicants are reminded that this application has been filed with informal drawings that are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(2) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(i), three sets of drawings or photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

Claim Objections

Claims 11 and 35 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 11 and 35 appear to merely specify characteristics that are already present in the nucleic acid sequence described by SEQ ID NO: 3, which is already present in the base claims from which claims 11 and 35 depend (i.e. claims 10 and 9, respectively).

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 14, 17-18, 35 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***These grounds of rejection are essentially the same as those made in Paper No. 24, mailed 9/13/01 and Paper No. 30, mailed***

6/17/03. The grounds for rejection are repeated below. A response to applicants' arguments follows the rejection.

Claims 1-6 are each drawn towards an isolated retrotransposon having a copy number of "between 40-150 or 50-100 copies" of itself per genome. The retrotransposon can be "free" or episomal, or the retrotransposon can be integrated. The retrotransposon can be isolated from fungi or yeast, or more specifically from Candida albicans. The broadest embodiments potentially encompass literally any eukaryotic cell type that might harbor a retro-transposable element (e.g. corn, yeast, human, fly, etc.). Even in more specific embodiments, the claims encompass any strain of Candida or, more specifically, Candida albicans. Each of the claims comprises the functional limitation of between 40 and 150 copies of itself per host cell genome.

The specification teaches one embodiment of the claimed invention (pCal or Tca2) which is found at high copy number in a few particular strains of C. albicans. No definitive explanation is provided in the specification for why pCal is maintained at such high copy number in these particular strains of C. albicans and not in others. For example, the mechanism could involve some mutation in pCal or a mutation in the particular host, or a combination of mutations in both the host and pCal. The prior art is of no help in describing a mechanistic rational for maintenance of such high copy numbers because the art does not appear to teach such numbers.

Given the large number of host cell types and retrotransposable elements potentially embraced by the rejected claims and the presence of the functional limitation for high copy number, the presence of only a single relevant example in the specification or prior art meeting the functional limitation for high copy number and the lack of teachings from the specification or prior art as to how such a high copy number is attained by the single relevant example, one of

skill in the art would not be able to envision a representative number of specific embodiments of the claimed invention to describe the potentially broad genus of such retrotransposable elements embraced by the rejected claims. Therefore, one of skill in the art would reasonably conclude applicants were not in possession of the claimed invention at the time of filing.

Response to Arguments/Written Description-"Free copies"

Applicant's arguments filed on 9/17/03 have been fully considered but they are not persuasive. The response essentially argues the amendment of the rejected claims to depend upon claim 12, which is purportedly limited to pCal (i.e. SEQ ID NO: 3), obviates the grounds of rejection.

If claim 12 were specifically limited to claim 12, the amendment would have obviated the grounds for rejection. Claim 12 is not, however, limited to pCal. Parts (b) and (c) encompass additional retrotransposon elements that can differ significantly from pCal (e.g. as little as 65% similarity with the LTR and POL regions of SEQ ID NO: 3 or hybridization under "stringent" conditions). Again, applicants' response and the instant specification have not provided a basis for envisioning those claimed embodiments that meet the functional limitation of being an extrachromosomal DNA molecule having 40-150 free copies per cell.

Claims 1-6, 12-14, 17-21, 35, 37-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is a new rejection made essentially for the same reasons as**

given in the office action mailed 6/17/03 (Paper No. 30). This rejection has been extended to additional claims due to applicants' amendment of the claims in the response filed 9/17/03.

The rejected claims comprise the limitation of a "...nucleotide sequence with at least 65% (or 70%, 75%, 80%, 85%, 90%, 95% or 97%) similarity with the LTR and POL region SEQ ID NO: 3...". The rejected claims read on literally any retrotransposon or nucleic acid fragment that comprises a sequence with the recited % similarity to SEQ ID NO: 3. This is an incredibly broad genus of retrotransposons and an even larger genus of nucleic acid fragments. The instant specification provides no basis for envisioning a representative number of embodiments of, for example, retrotransposons that are only similar at a 65% level with only part of the transposon sequence. The instant specification provides no basis for one of skill in the art to envision nucleic acid fragments that are only 65%-97% similar to the LTR and POL regions of SEQ ID NO: 3 and which retain any sort of retrotransposon activity. Similarly, the specification provides no basis for one to envision embodiments of the claims nucleic acid fragments that retain any of the asserted utilities for the nucleic acid fragments of the invention (e.g. as specific probes for pCal and/or Candida species). As pCal appears to be novel in the art, the prior art does not offset the deficiencies of the instant specification with regard to providing a basis for envisioning a sufficient number of specific embodiments as to describe the broadly claimed genus. Therefore, one of skill in the art would have reasonably concluded applicants were not in possession of the claimed invention.

Claim 19, part (a), is further directed to "...a nucleic acid sequence positioned between at least two terminal repeats of the sequence of pCal as described in GenBank accession number

AF007776...". Claim 19, part (c), recites a nucleic acid sequence that hybridizes under "stringent" hybridization conditions to the nucleic acid sequence of part (a). The metes and bounds of part (a) are unclear and can be interpreted to encompass literally any nucleic acid sequence sandwiched between the LTR sequences of pCal. The metes and bounds of what constitutes "stringent" hybridization conditions are unclear and undefined in the instant specification, allowing the skilled artisan to read the rejected claims as encompassing almost any hybridization conditions. For these reasons, there is no basis for the skilled artisan to envision a representative number of embodiments of such nucleic acid sequences. Therefore, the skilled artisan would reasonably have concluded applicants were not in possession of the claimed invention.

Response to Arguments/112 1st Written Description-% Identity

Applicant's arguments filed in the response of 9/17/03 have been fully considered but they are not persuasive. The response essentially argues 1) the specification describes SEQ ID NO: 3, 2) stringent hybridization conditions were conventional in the art at the time of filing, 3) the claimed nucleotide of claim 12 is described functionally and structurally by sequence identifier, hybridization conditions and percent identity, 4) a person of skill in the art would not expect substantial variation among species of DNAs encompassed by the rejected claims, 5) Example 14 of the Written Description Guidelines describe a fact pattern that is directly analogous to the instant claims, 6) according to Example 14, even if SEQ ID NO: 3 is the only species disclosed, it is representative of the claimed genus because all members of the genus

have a specified level of identity with the disclosed species and retain a specified function (e.g. claim 12 is directed to a retrotransposon).

Arguments directed to what was conventional in the art at the time of filing concerning "stringent" hybridization conditions are not persuasive because the exact metes and bounds of the term "stringent hybridization" were not art accepted at the time of filing and the specification does not provide an explicit definition of what is encompassed by the term (e.g. see the rejection under 112 2nd paragraph below). Any arguments dependent upon what was art recognized concerning "stringent hybridization conditions" are thus moot.

With regard to the guidance given by Example 14 of the Guidelines, the examples given in the guidelines are presented for guidance and are not necessarily limiting. For example, a recited function in this case of being a "retrotransposon" (claim 12 and dependent claims) requires retention of structural/functional characteristics within the retrotransposon described by SEQ ID NO: 3. Alternatively, in order for a claimed nucleic acid fragment to possess at least one of the asserted utilities described in the instant specification (e.g. use as a probe for SEQ ID NO: 3 and/or strains of Candida), it must retain certain structural/functional elements of the claimed invention. As the instant specification has provided little or no guidance with regard to what changes can be made to the nucleotide sequence described by SEQ ID NO: 3 such that the nucleic acid comprising the changes retains functional activity, there remains no basis for the skilled artisan to envision specific embodiments of the claimed invention such that the broadly claimed genus is described. For these reasons, description of SEQ ID NO: 3 alone is not sufficient to describe the broadly claimed genus of retrotransposons and/or DNA fragments.

Claims 1-6, 12-14, 17-21, 35, 37-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments limited to the retrotransposable element pCal or TCa2 (i.e. as described by SEQ ID NO: 3), or nucleic acid fragments thereof, does not reasonably provide enablement for embodiments wherein the retrotransposable element is other than pCal or TCa2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected claims are all directed to a retrotransposable element and/or DNA fragment designated pCal (episomal form) or TCa2 (integrated form) described by SEQ ID NO: 3, or variants thereof retaining the structural/functional characteristics of a retrotransposable element.

Breadth of the claims: The base claims (claims 12 and 19) encompass embodiments that 1) comprise a nucleotide sequence with at least 65% (or 70%, 75%, 80%, 85%, 90%, 95% or 97%) similarity to the LTR and POL regions of SEQ ID NO: 3 (present in deposit AF007776), 2) nucleic acids that hybridize to either SEQ ID NO: 3, or 3) hybridizes under stringent conditions to a nucleic acid sequence sandwiched between at least two of the terminal repeat sequences of the nucleic acid deposited in GenBank as AF007776. The "stringent" hybridization conditions

have not been explicitly defined and can be broadly read to encompass almost any hybridization conditions. Thus, the rejected claims encompass an enormously broad genus of retrotransposable elements and/or nucleic acid fragments that must either function as retrotransposable elements (e.g. claim 12) or function in some utility that corresponds to the asserted utilities for pCa1 or TCa2.

Functionally, several of the claims recite the limitation that the retrotransposable element is found as an extrachromosomal DNA molecule having a copy number of 40-150 free DNA copies per cell. This greatly exacerbates the complexity of the claimed invention as it requires at least some understanding as to how pCal maintains such a high copy number of itself in the host cell.

Guidance of the specification/The existence of working examples: The instant specification teaches the isolation and general characteristics of a retrotransposable element from *Candida albicans* termed pCal in its extrachromasomal form and TCa2 in its integrated form. Remarkably, pCa1 is maintained at ~40-150 "free" copies of itself per cell, as well as in an integrated form. The specification teaches that portions of pCa1 can be used as probes to identify pCa1 or TCa2, and/or to identify strains of Candida comprising the retrotransposable element.

The specification does not teach, however, what portions of SEQ ID NO: 3 are required for retrotransposon activity, much less what portions are required for maintaining 40-150 episomal copies per cell.

State of the art/Predictability of the art: The retrotransposable element described by SEQ ID NO: 3 (pCa1 or TCa2) appears to have been novel in the art at the time of filing. It

appears to have been novel in the art as well with regard to its ability to maintain such high copy numbers of itself in the host cell in a stable, episomal manner. Therefore, the prior cannot offset the deficiencies of the instant specification with regard to those elements of SEQ ID NO: 3 required for functional activity.

Given the broad genus of retrotransposable elements and nucleic acid fragments encompassed by the rejected claims, and given the lack of significant teachings in the prior art concerning the functional/structural characteristics of SEQ ID NO: 3, making and using the claimed invention in the broad scope encompassed by the rejected claims would necessarily have been unpredictable, requiring trial-and-error experimentation.

The amount of experimentation necessary: Given the combination of the factors outlined above, it would have required undue, unpredictable experimentation in order to make and use the invention commensurate in scope with the rejected claims. For example, for embodiments wherein the nucleic acid is required to retain retrotransposon activity, one would have had to first envision possible changes to the sequence described by SEQ ID NO: 3 (~6 kb in length) that might retain functional activity, construct nucleic acids comprising the activity, and test such recombinant constructs to determine that the resulting structure retained the ability to function as a retrotransposon in a given host cell. Alternatively, for embodiments where the nucleic acid is used to probe for the presence of SEQ ID NO: 3 in a host cell, one would have first had to envision changes to SEQ ID NO: 3 that would allow the resulting nucleic acid to retain the ability to bind to SEQ ID NO: 3 in a specific manner, construct such nucleic acid fragments, and then test the fragments to see if the recombinant nucleic acids retain the ability to bind to SEQ ID NO: 3 in a specific manner such that the nucleic acid could be used a probe for a host strain

comprising pCal or TCa2. In either case, the experimentation required would have to have been trial-and-error in nature and would necessarily have been undue given the combination of the factors outlined above. Therefore, the instant specification is found to be enabling only for those embodiments directed to SEQ ID NO: 3 or fragments thereof.

Claim Rejections - 35 USC § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 9-14, 17-21, 35-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-10 are vague and indefinite in that it is unclear as to whether the claimed transposable element is limited to SEQ ID NO: 3, or can further comprise additional elements. **This is a new rejection.** For example, the claimed transposable element is specified as "having the sequence identified as SEQ ID NO: 3", but also comprising an "internal" domain for receiving a nucleotide sequence encoding a desired protein. Is the "internal domain" necessarily found *within* SEQ ID NO: 3, or can it be somehow external to SEQ ID NO: 3?. Similarly, does the term "having" specify that the transposable element "comprises" SEQ ID NO: 3, or does it mean that the transposable element "consists essentially of" SEQ ID NO: 3?

Claim 13 is vague and indefinite in that the metes and bounds of the phrase "...the integrated form of the retrotransposon in claim 12..." are unclear. First, there is no clear and positive prior antecedent basis for the term "integrated form" in claim 12, upon which claim 13

is directly dependent. Second, it is unclear how the claimed "integrated form" can be isolated and purified, as recited in claim 12, if it is integrated into a host genome. **This is a new rejection.**

Claim 19 is vague and indefinite in that the metes and bounds of the phrase "...a nucleic acid sequence positioned between at least two terminal repeats of the sequence of pCal as described in GenBank accession number AF007776..." are unclear. **This is a new rejection.** It is unclear whether the claim is limited only to the transposable element found in AF007776 (i.e. pCal), or whether it is also directed to literally *any* nucleic acid sequence sandwiched between the LTR's found within the transposable element found in AF007776. It would be remedial to amend the claim language to clearly indicate whether part (a) is directed solely to pCal, or encompasses any DNA sequence sandwiched between the LTR's of pCal.

Claims 12 and 19 are vague and indefinite in that the metes and bounds of the phrase "...hybridizes under stringent conditions..." are unclear. **This rejection is maintained for reasons of record repeated here.** The phrase is unclear in that the term "stringent hybridization conditions" is not clearly defined in the specification. The concept of what qualifies as "stringent" conditions is likely to vary from investigator to investigator, and is highly subjective. It would be remedial to amend the claim language to explicitly recite the "stringent" hybridization conditions (i.e. salt conditions, temperature, etc.).

Response to Arguments/112 2nd Rejection-"Stringent Hybridization Conditions"

Applicant's arguments filed 9/17/03 have been fully considered but they are not persuasive. The response essentially argues that "stringent" hybridization conditions were

described in the instant specification (e.g. pages 26-28) and that the term is well known and understood in the art.

The specification merely cites a couple of prior art references where different hybridization conditions are taught. However, there remains no explicit definition in the specification as to what such conditions necessarily encompass so that the skilled artisan cannot rely on the specification to determine the metes and bounds of the term. Second, the assertion that the term is well known and understood in the art is not supported and implies that a specific set of conditions were art recognized as being "stringent" hybridization conditions. As stated in making the rejection, such "stringent" hybridization conditions are and were likely to vary from investigator to investigator and are, therefore, vague and indefinite unless explicitly defined by the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13, 19-21 and 44-50 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. **This is a new ground of rejection.**

Each of the rejected claims can be interpreted to read on copies of pCal or Tca2 found in nature. Thus, the claims read on products of nature. It would be remedial to amend the claims to somehow show the "hand of man" (e.g. an "isolated" or "recombinant" retrotransposon).

Allowable Subject Matter

Claims limited to SEQ ID NO: 3 and fragments thereof appear to be allowable over the prior art and meet 112 1st requirements. Claim 13 appears to be the only claim that is nearly limited in such a fashion to SEQ ID NO: 3, but has further problems under 35 U.S.C. 112 2nd paragraph and 35 U.S.C. 101.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr., PhD
Primary Examiner
Art Unit 1636

GERRY LEFFERS
PRIMARY EXAMINER

Ggl